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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/393,023	09/09/1999	PAUL S. MEISSNER	PF-200	2146

22195 7590 06/18/2003  
HUMAN GENOME SCIENCES INC  
9410 KEY WEST AVENUE  
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EXAMINER

SPECTOR, LORRAINE

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 06/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.



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APPLICATION NUMBER	FILED DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
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EXAMINER
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ART UNIT	PAPER NUMBER
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DATE MAILED:

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

### OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 4/4/03

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claims

- ☒ Claim(s) 21-28, 33-40, 42-53, 69-75, 80-114 is/are pending in the application.  
Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☒ Claim(s) 21-28, 33-40, 42-53, 69-75, 80-114 is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☐ Claim(s) \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

- ☒ Notice of Reference Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s) \_\_\_\_\_
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

Best Available Copy

### **DETAILED ACTION**

Claims 21-28, 33-40, 42-53, 69-75, and 80-114 are pending and under consideration.

The rejection of claims 21, 29-33, 35-38 and 41-83 under 35 U.S.C. § 112, first paragraph is withdrawn in view of applicants amendments.

The rejection of Claims 37, 45, 47-69, 72, 74-80, 83, 85, 89, 91 and 95 under 35 U.S.C. 112, second paragraph is withdrawn in view of applicants amendments.

### ***Objections and Rejections under 35 U.S.C. §§101 and 112***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 21-28, 33-40, 42-53, 69-75, and 80-114 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility for reasons set forth in the previous Office Action at pages 2-4. Applicants traversal in paper number 29 submitted 4/4/03 has been fully considered but is not deemed persuasive.

Applicants argue that an incorrect standard has been applied, i.e. that the examiner has not met the burden of showing that it is more likely than not that the claimed protein cannot be used as a cancer marker as claimed. This argument has been fully considered but is not deemed persuasive because the point in the rejection as made is that the person of ordinary skill in the art would not consider the assertion that the claimed protein can be used as a cancer diagnostic to be substantial. The specification merely asserts that "The criptin growth factor is overexpressed and secreted by certain types of cancer cells, for example, by pancreatic cancers", (page 2), a statement which is reiterated at page 17. This is not a substantial assertion of utility.

"Pancreatic cancers" is an exemplary recitation, however, such would presume that all pancreatic cancers are created equal, which they are not. Cancer is not a single disease, but rather a functional definition of diseases characterized by malignant, uncontrolled cell growth. Applicants disclosure at pages 2 and 17 constitutes a mere invitation to experiment to determine what cancers, if any can be diagnosed by assaying levels of criptin protein. The specification discloses no information as to what a "normal" level of criptin protein is, nor what levels would be diagnostic of cancer, nor of what specific types of cancer such levels would be diagnostic. Further, the assertion of utility for diagnosis of cancer is, as stated in the previous Office Action, predicated on "An initial Northern blot analysis [that] has shown very high expression in pancreatic cancer cells." As previously stated, polynucleotide expression is not necessarily indicative of protein expression. There is no information on altered level of protein (the claimed product) in pancreatic cancer cells. Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12:82-88). The data presented in the specification were not corrected for aneuploidy. An amplification of a gene does not necessarily mean overexpression in a cancer tissue, but can merely be an indication that the cancer tissue is aneuploid, or that there is an amplification of the portion of the chromosome bearing the criptin gene. The preliminary data were not supported by analysis protein expression, and thus would not be considered by the person of ordinary skill in the art to be a substantial assertion, but rather a speculative one. Thus, the data do not support the assertion that criptin can be used as a cancer diagnostic. Significant further research would have been required of the skilled artisan to determine whether criptin is overexpressed in cancer *to the extent that it could be used as a cancer diagnostic*, and in which cancers it is so overexpressed, and thus the implicitly asserted utility is not substantial, but rather requires substantial further experimentation.

Applicants have asserted that the overexpression of criptin protein was found in cancer cells, as opposed to cancer cell lines, and that thus the issues regarding cancer cell lines are moot. This assertion is noted, however it does not obviate the primary basis for the rejection, namely that based upon the disclosure in the specification as originally filed, the person of ordinary skill in the art would not consider the assertion that the criptin protein can be used for the diagnosis of

cancer, without substantial further experimentation to determine which types of cancer and how, to be credible.

Applicants argument that the fact that the criptin gene was isolated from a pancreatic cancer tissue cDNA library supports the assertion of utility has been fully considered but is not deemed persuasive because many genes are expressed in cancerous tissue that are also expressed in normal tissue, and there is no indication that the gene (protein) was preferentially expressed in that cDNA library, nor that any technique such as subtractive hybridization had been performed to enrich for cancer-specific proteins. Further, even if the criptin gene had been overexpressed in that cDNA library, that fact alone would not be considered by the person of ordinary skill in the art to be sufficient to make substantial the assertion of diagnostic utility. The state of the art is that confirmation of the association between overexpression of the protein and specific types of cancer, including characterization of "normal" and "diagnostic" expression levels would be required. For example, see Clark et al., Brit. J. Cancer 81:1002, who analyzed expression of a target gene, PIP, in 97 independent primary breast tumors, confirmed the nucleic acid results with immunohistochemistry, and studied and disclosed normal levels of expression of PIP, and then concluded that PIP "has *potential* as a marker of breast micrometastasis" (emphasis added, see page 1007, 1<sup>st</sup> col.). Clark et al. demonstrate the state of the art, which is that the person of ordinary skill in the art would not conclude that a protein had utility as a cancer diagnostic based upon a northern blot from a single isolate.

Thus, based upon the information proffered in the specification as originally filed, the person of ordinary skill in the art would have to determine (a) whether there is a positive correlation between criptin levels and pancreatic cancer (b) determine what those diagnostic levels are and (c) what types of pancreatic cancer display those diagnostic levels, (d) determine how to obtain samples to test those levels (i.e. pancreatic biopsy, serum assay, etc.)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-28, 33-40, 42-53, 69-75, and 80-114 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

***Claim Rejections - 35 USC § 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR

1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

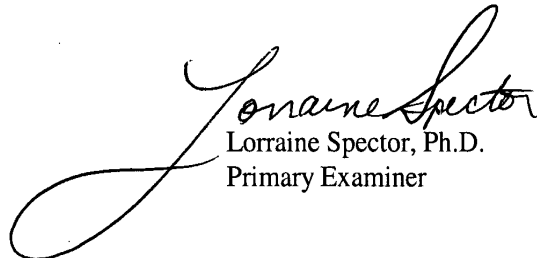
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.

  
Lorraine Spector, Ph.D.  
Primary Examiner

09/393023.2

6/12/03